REMARKS

Claims 1-10 and 16-19 are presently pending in the application. Claims 1-10 and 16-19 stand rejected. Claim 1 has been amended to recite a method performed in a liquid sample and optionally in the presence of a chelator. Support for these amendments can be found, e.g., at page 7, lines 16-24 and at page 16, Example 1. Claims 3 and 5 have been amended to correct an obvious spelling error. It is believed that these amendments do not constitute new matter and their entry is requested.

35 U.S.C. 112 first paragraph rejections

The Examiner has maintained the rejections of claims 1-10 and 16-19 for lack of enablement under 35 U.S.C. § 112, first paragraph.

At paragraph 2 of the Detailed Action, the Examiner asserts that the claimed invention will not distinguish between the presence of tetracycline in the medium and background luminescence. The Examiner is apparently of the opinion that the claimed methods would attribute any increase in signal to the presence of tetracycline, even if the increase was not statistically significant. Specifically, the Examiner states at page 2 that "[a]s presently worded, the observation of any increase in signal, even if it is not statistically significant, is to be interpreted as being indicative of Tetracycline being present when in fact no tetracycline would be present." This is not the case. In fact, the claims specifically recite that a detectable luminescence higher than a luminescence of the control cells indicates the presence of tetracycline. Inherent in this phrase, as would be instantly recognized by one of ordinary skill in the art, is the concept of establishing the level of background luminescence that can occur in control cells present in a liquid lacking tetracycline. That is what the control cells are for and that is how they are described in the specification (See, e.g., Figures 4-11) and recited in the claims. Example 1 specifically demonstrates the sensitivity of the assay using a serial dilution of tetracycline. As recited in claim 1, the luminescence detected in test cells is compared to the luminescence in control samples and wherein detectable levels of luminescence higher than the luminescence seen in control is indicative of the presence of tetracycline in the medium. It is respectfully submitted that one of ordinary skill in the art would readily recognize that a level of luminescence higher than control would be significant.

The Examiner goes on to assert that "changes in background signal would be interpreted as being a positive signal for the presence of tetracycline." In response, Applicants are unaware of any teaching in the present disclosure that teaches or suggests that changes in background would be interpreted as a positive signal. Nor, as discussed above, do the claims recite a method wherein changes in background signal are interpreted as being a positive signal for the presence of tetracycline. Quite the contrary, the claims recite a method wherein only a "detectable luminescence higher than a luminescence of the control cells" is interpreted as being positive for the presence of tetracycline. The claims recite a reproducible procedure whereby one could indeed determine the presence of tetracycline when the difference between luminescence between samples and controls is detected. By its very nature, anyone of ordinary skill in the art would realize that the reliability of the result would be dependent on the amount of increase of luminescence compared to background. The ability to distinguish between background in controls and positive reaction in tested samples is a well established concept which has been routinely performed for decades when employing numerous assays. This assessment would address the limit of detection, accuracy, specificity and reproducibility in the context of the specific assay. It is respectfully submitted that it requires no undue experimentation to establish a threshold level which determines when a sample is luminescing greater than background levels. It is worth noting that the level of distinction between background and positive reactions will by nature vary depending on the required accuracy of a test. For example, if the test is a preliminary screen that will be followed up with a secondary more sensitive assay, a minimal number of false positives can readily be tolerated.

In order to sustain an enablement rejection, the "examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention." MPEP2164.04, citing In re Wright, 999 F.2d 1557, 1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993). Furthermore, it is incumbent upon the Patent Office to "explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." MPEP 2164.04, citing In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA

1971). Furthermore, while references may not be required for the Examiner to meet his or her burden, "specific technical reasons are always required. Id., emphasis added.

The Examiner has not met the burden imposed in the MPEP under the applicable statutes. Instead he has simply asserted that the specification does not teach how to distinguish between background and positive samples. In support of this assertion, the Examiner has not cited to the specification, a scientific reference, or to any scientific or technical facts known to those of ordinary skill in the art. In sum, there is no specific technical reasoning provided to support the Examiner's contention that the claimed assay can not or will not distinguish between background luminescence and luminescence in response to tetracycline. In contrast, the specification recites numerous examples where the level of background luminescence is clearly distinguishable as lower than the luminescence seen in positive reactions. (See, e.g., Example 2 at page 17 and Figures 4-11).

At paragraphs 3 and 5-7, the Examiner asserts that the system has not been demonstrated to enable expression and detection of luminescence in any strain of microbe other than the single *E. coli* strain in the present examples. After noting the use of a single strain, the Examiner notes that the specification states that the assay is "ineffective" when Ca+ and Mg+ ions are present, the claims read on any sample and thus the claimed "method cannot be practiced with any sample." (Top of Page 4, Paper No.21). The Examiner has thus asserted that the claimed method will not work in the presence of magnesium or calcium ions and thus is not enabled. The claims have been amended to recite a method wherein a chelator is present in the liquid sample. The Examiner also again notes that the Examples only describe practice of the claimed method in one strain and with one DNA construct. It is respectfully submitted that no working examples are even required and, absence some technical reason as to why the claimed method would not work, the claims must be allowed as enabled. The Examiner has offered no scientific or technical support as to why the claimed methods as amended could not be practiced in any strain without undue experimentation.

In view of the amendments to the claims and above arguments, it is believed the claims are in condition for allowance and Applicants request that the rejection of the claims under 35 U.S.C. § 112, first paragraph for lack of enablement be withdrawn.

35 U.S.C. 112 second paragraph rejections

The Examiner has also rejected the claims as indefinite, based on the recitation of liquid from a liquid or solid sample. Claim 1 has been amended to recite an assay based on a liquid sample.

The Examiner has also found the claims indefinite for reciting the limitation of a "higher" luminescence. The Examiner states at page 4 of Paper No. 21 that the term "'higher' is a relative term...[and]...the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention."

According to the MPEP, 2173.05(b), the acceptability of relative "claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification." As discussed in detail above, the claims recite methods wherein a detectable luminescence level higher than a luminescence of the control cells indicates the presence of tetracycline in the sample. The term higher is in fact defined directly in the claim as a level higher than the level of luminescence in control cells. Furthermore, as also discussed in detail above, the Examples and Figures are replete with distinctions between control levels of luminescence and positive levels. Thus, anyone of ordinary skill in the art would instantly realize that control cells would have a range and anything above that range would represent a level "higher" than controls and would thus have no difficulty in understanding the scope of the claimed invention.

In view of the amendments to the claims and above arguments, it is believed the claims are in condition for allowance and Applicants request that the rejection of the claims under 35 U.S.C. § 112, second paragraph for being indefinite be withdrawn.

CONCLUSION

In view of the above amendments and remarks, it is believed that the claims satisfy the requirements of the patent statutes and reconsideration of the instant application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

RESPECTFULLY SUBMITTED,					
NAME AND REG. NUMBER	Michael J. Moran, Ph.D., Registration No. 42,013				
SIGNATURE	Michael J Moran		DATE	6/6/03	
Address	Rothwell, Figg, Ernst & Manbeck 1425 K Street, N.W.				
City	Washington	*State*	D.C.	*Zip Code*	20005
Country	U.S.A.	*Telephone*	202-783-6040	*Fax*	202-783-6031

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